REMARKS

Applicants have carefully studied the Office Action mailed on October 2, 2006. The present amendments and remarks are intended to be fully responsive to all points of rejection raised by the Examiner and are believed to place the claims in condition for allowance. Favorable reconsideration and allowance of the present claims are respectfully requested.

A substitute specification is submitted herewith. Also submitted is a marked up copy of the new specification showing the changes between the newly submitted specification and that submitted on September 19, 2005. In the new substitute specification, the title has been changed to that suggested by the Examiner, i.e., to "Method of Regulating Hematopoietic Cell Survival," and the residue numbers recited therein have been corrected in accordance with SEQ ID NO:1. No new matter has been added.

All citations to the specification in this response are to the specification of record submitted on September 19, 2005.

Status of the claims

Claims 73-75, 78 and 79 have been amended. Support for these claim amendments can be found at, for example, the original claims and page 32, lines 25-27 of the specification. No new matter has been added. Claims 73-79 are pending and at issue.

Enablement rejection

Claims 73-79 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that claims 73-79, while being enabled for "decreasing hematopoietic cell survival *in vitro* [when] the sequence ^{598}HSRSLP^{603} of SEQ ID NO: 1 [is mutated] to ^{598}EFAAAA^{603} (or by truncating the receptor as taught by the prior art)," are not enabled for (1) other mutations of the binding motif, (2) . . . increasing hematopoietic cell survival, or (3) . . . regulating hematopoietic cell survival *in vivo*."

This rejection is respectfully traversed, and reconsideration is respectfully requested.

The Examiner acknowledges that "the claims are enabled for a method of *decreasing* hematopoietic cell survival *in vitro* by mutating the ^{598}HSRSLP^{603} binding motif of a receptor of SEQ ID NO: 1 to the sequence ^{598}EFAAAA^{603}. . . . " (Office Action, dated October 2, 2006, page 4, second full paragraph) (emphasis added).

In order to expedite prosecution, claim 73 has been amended to recite a method of *inhibiting* hematopoietic cell survival consisting of mutating at least one of the residues of a binding motif of a GM-CSF/IL-3/IL-5 receptor of a hematopoietic cell.

Applicants submit that *in vitro* activity as measured by the assay in Example 8 is predictive of *in vivo* activity, as the same part of the cell signaling transduction pathway is effected in each instance (*see* Response, dated June 20, 2006, page 5, second and third full paragraphs, for a description of the cell survival pathway). To this end, Example 4 also shows that mutation of the claimed binding motif results in *in vivo* inhibition of the phosphorylation required for signal transduction that, in turn, inhibits cell survival (specification, page 40, line 8 to page 41, line 9).

Applicants also submit that those of skill in the art would have been able to create the claimed binding motif mutations using methods already generally known in the art (*see, e.g.*, specification, Example 1(a) on page 35, lines 15-28). Accordingly, applicants need not disclose the details regarding construction of the mutated binding motifs as "[i]t is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art . . . ." *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Further, once mutated, the assays described in the specification can be used to determine whether the binding at the motif has been disrupted and whether cell survival can be effected (*see* specification, page 21, lines 28-34 (noting that "electrophoretic mobility shift assays (EMSA or band assays) or foot print assays or pull down experiments are available to measure specific binding"); Examples 8-9, page 46, line 20 to page 48, line 32 (disclosing effect that mutation of the binding motif has on cell survival)).

Thus, the claims are enabled as one of ordinary skill in the art would not have to undertake undue experimentation to make the claimed mutated proteins which inhibit *in vivo* hematopoietic cell survival. Accordingly, applicants respectfully request withdrawal of this rejection.

Indefiniteness

Claims 73-79 have been rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. The Examiner contends that claim 73 (1) omits essential method steps as the recited steps do not achieve the stated goal of regulating hematopoietic cell survival, (2) is unclear as to how targeting a mutation to a binding motif relates to the goal of regulating hematopoietic cell survival, and (3) is unclear as to what is meant by the phrase "a cytoplasmic protein of a GM-CSF/IL-3/IL-5 receptor." With regard to claims 74 and 75, the Examiner contends that it is not clear if the serine or threonine residue(s) in the claims are present in the binding motif before or after mutation of the motif.

This rejection is respectfully traversed, and reconsideration is respectfully requested.

In order to expedite prosecution, claims 73-75 have been amended to recite a method of inhibiting cell survival rather than a method of regulating cell survival. Further, the specification explains that *the claimed mutation inhibits cell survival by inhibiting the phosphorylation required for signal transduction* (specification, page 47, lines 31-32 (noting that the ability to phosphorylate "is important for maintaining cellular viability")). Example 4 of the specification shows that mutation of the binding motif results in *in vivo* inhibition of the phosphorylation required for signal transduction (specification, page 40, line 8 to page 41, line 9).

The phrase "or threonine" has been removed from amended claim 74 and claim 75 has been amended to clarify that the claimed binding motif includes mutation of the "two (2) amino acids."

For these reasons, applicants respectfully request withdrawal of this rejection.

Anticipation

Claims 73-79 have been rejected as anticipated by Stomski et al., "*Identification of a 14-3-3 Binding Sequence in the Common β Chain of the Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), Interleukin-3 (IL-3), and IL-5 Receptors That is Serine-Phosphorylated by GM-CSF*," Blood 94:1933-1942 (1999) ("Stomski") and Smith et al., "*Cytoplasmic domains of the common beta-chain of the GM-CSF/IL-3/IL-5 receptors that are required for inducing differentiation or clonal suppression in myeloid leukaemic cell lines*," EMBO 16:451-464 (1997) ("Smith").

This rejection is respectfully traversed, and reconsideration is respectfully requested.

1. Stomski

Submitted herewith is a declaration by the applicants stating that they are the sole inventors of the presently claimed invention and that the other co-authors (M. Dottore, W. Winnall, J. Woodcock, C.J. Bagley, D.T. Thomas and R.K. Andrews) listed on the Stomski article were merely working under their direction and did not contribute to the conception of the presently claimed invention (Declaration at ¶ 6).

As the Stomski article was published by the present inventors within one year of the U.S. filing date of the PCT application from which this application claims priority, Stomski is not prior art under 35 U.S.C. § 102(a) to the present application. MPEP §§715.01(c) and 2132; *In re Katz*, 687 F.2d 450 (CCPA 1982). Accordingly, applicants respectfully request that the rejection be withdrawn.

2. Smith

The Examiner contends that the residues disclosed by Smith correspond to the those used in SEQ ID NO: 1 of the instant application. According to the Examiner, Smith teaches a truncated

ß-chain that includes a deletion of residues 598-603 of the wild type receptor and that this truncated ß-chain does not support the growth of transfected CTLL2 cells.

Smith teaches the deletion of entire segments of the ß-chain ranging in size from 114 to 436 amino acid residues but does not specifically indicate the importance of the claimed ^{598}HSRSLP^{603} sequence. That is, Smith does not disclose or suggest the claimed binding motif having an amino acid sequence according to SEQ ID NO: 1 and one or more mutations in the ^{598}HSRSLP^{603} sequence. Further, in contrast to the truncated ß-chains disclosed in Smith, the length of the amino acid sequence according to SEQ ID NO: 1 is largely maintained despite the claimed mutation(s) of the ^{598}HSRSLP^{603} sequence.

Accordingly, Smith does not teach or suggest a mutation at the specifically claimed ^{598}HSRSLP^{603} sequence and, thus, does not anticipate the claimed invention. Applicants, therefore, respectfully request withdrawal of this rejection.

CONCLUSION

In view of the above amendments and remarks, it is respectfully submitted that the pending claims are now in condition for allowance and such action is earnestly solicited. If the Examiner believes that a telephone conversation would help advance the prosecution in this case, the Examiner is respectfully requested to call the undersigned attorney at (212) 527-7601. The Examiner is hereby authorized to charge any additional fees associated with this response to our Deposit Account No. 04-0100.

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Respectfully submitted,

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